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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,293	11/17/2003	Stephen P. Massia	049954-004100	8809

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EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,293	MASSIA ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *102,105 and 106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *102,105-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/14/10 has been entered.

Applicants amendments and arguments filed 3/4/10 are acknowledged and have been fully considered.

The original restriction requirement was sent out 7/3/06. On 3/12/07 (as noted in the office action dated 1/7/08) applicants elected group I and the species of SEQ ID NO:124.

In the instant case, the prior art obviate the elected species. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species.

Claims 1-101,103-104 have been cancelled.

Claims 102,105-106 are under consideration.

Claim Rejections - 35 USC § 103

Claims 102,105-106 were previously rejected under 103 based on the references cited below. Since the claims have been amended the rejection is updated.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 102,105-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rieu et al (Journal Cell Biology 1994 v127 pages 2081-2091 as cited in IDS 11/10/04) and Laplantine et al (Journal of Cell Science 2000 v113 pages 1167-1176; first cited with office action 5/11/09).

Rieu teach that the A-domain of beta2 integrin CR3 is a receptor for the hookworm-derived neutrophil adhesion inhibitor NIF (abstract). Rieu teach that integrins contain binding sites for protein ligands that play essential roles in leukocyte trafficking for example (abstract). Rieu map the NIF binding site to the A-domain and to specific peptide regions (abstract). Rieu teach (page 2086,2089) that the A-domain protein (i.e. r11bA) was immobilized and particular peptides were tested for their ability to inhibit NIF binding. One of the peptides tested (A7 figure 6) corresponded to residues 232-245 and had the amino acid sequence NAFKILVVITDGEK. Rieu teach that the binding site comprised primarily peptide A7 (page 2089 first sentence of first

complete paragraph, Figure 6). Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2nd column).

Rieu does not expressly teach a peptide of SEQ ID NO:124

Rieu does teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract). Rieu teach that the A-domain may be useful for treating hookworm infections and state that the A domain is a target for anti-inflammation therapeutics (page 2090). Thus one would be motivated to identify the A-domain. Rieu also notes that certain peptides did not absorb adequately (page 2086 first paragraph last sentence). Rieu teach that numerous peptides could not be tested because the peptides did not adequately bind to plastic wells (page 2086). Thus one would be motivated to use alternative assays that allow for adequate immobilization of the peptides.

Laplantine also teach about interactions between integrins and other proteins (title, abstract). Like Rieu, Laplantine recognize that integrins play an important role in triggering intracellular signaling (page 1167, page 1174). Laplantine investigate the interactions between a beta1 integrin and an alpha3 integrin (abstract). Laplantine specifically use surface plasmon resonance to investigate the interaction (page 11169 section 'surface Plasmon resonance, pages 1172-1173, Figure 7). Specifically, Laplantine teach that peptides corresponding to the beta1 subunit and containing an additional N-terminal cysteine residue were immobilized on a dextran through thiol coupling (page 1173 first column). The immobilized peptides were then exposed to peptides corresponding to alpha subunits and binding profiles were recorded (page 1173 first column).

Since Rieu teach investigating the interaction between an integrin and a possible interacting partner one would be motivated to use known techniques that are used to investigate such interactions. Since Rieu teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract) and that the A-domain may be useful for treating hookworm infections and that the A domain is a target for anti-inflammation therapeutics (page 2090) and that certain peptides did not absorb adequately (page 2086 first paragraph last sentence) one would be motivated to further study the A-domain NIF interaction. Rieu teach that numerous peptides could not be tested because the peptides did not adequately bind to plastic wells (page 2086). Since Laplantine teach surface plasmon resonance as a specific method to investigate integrin interactions one would be motivated to use the method of Laplantine with a reasonable expectation of success. Since Laplantine provide a specific example (see Figure 7) one would have a reasonable expectation of success. Laplantine teach (page 1174) that the surface plasmon resonance indicated interactions between integrin peptides and other subunit peptides. Thus one would have a reasonable expectation of success that the method would be able to indicate interactions between an integrin and an interacting partner as in the peptides of Rieu.

Since Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK) (page 2089 first sentence of first complete paragraph, Figure 6) one would be motivated to use such peptide as the sequence to attach to the dextran. Since Laplantine teach that the dextran is attached via thiol coupling to an additional N-terminal cysteine residue (page 1173 first column) one would be motivated to add an N-terminal cysteine to peptide A7 of Rieu to obtain CNAFKILVVITDGEK and then couple the dextran. The resulting product would

be the peptide CNAFKILVVITDGEK (which is SEQ ID NO:124 of the instant invention) covalently attached by thiol coupling to a dextran thus meeting the limitations of claims 102,105-106 of the instant invention.

It is noted that the instant claims recite 'bioconjugate consisting of'....'comprising'. In the instant case, the conjugate obviated by the prior art (i.e. the peptide CNAFKILVVITDGEK covalently attached by thiol coupling to a dextran) meets the claim limitations. Further, it is noted that section 2111.03 of the MPEP discusses transitional phrases (see In re Crish, 393 F.3d 1253, 73 USPQ2d 1364 (Fed. Cir. 2004)).

It is noted that claims 102 and 105 recite wherein clauses that recite functional properties. In the instant case, the prior art expressly teach the hydrophilic polymer/polysaccharide as recited in claim 106. Thus there is a reasonable basis that the polysaccharide has the recited function. Further, the prior art suggest the peptide sequence as recited in claims 1-2,105. Thus there is a reasonable basis that the peptide has the recited function.

In the instant case, both Rieu and Laplantine are drawn to methods of identifying interacting regions between integrins and interaction partners. Rieu teach a method in which peptides were adsorbed to plastic wells but notes that numerous peptides did not absorb adequately (page 2086 first paragraph). Laplantine teach a method in which selected peptides containing an additional N-terminal cysteine were immobilized on dextran through thiol coupling and used as part of a surface plasmon resonance analysis. The claims would have been obvious because a particular known technique (i.e. surface plasmon resonance) was recognized as part of the ordinary capabilities of one skilled in the art. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of

success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Arguments 103 rejection

Applicants argue (pages 3-6) that the examiners assertion is no more than an invitation to try and there is no indication of which parameters were critical and there is no direction as to which of many choices were likely to be successful.

Applicants argue that there is no reasonable expectation of success regarding ICAM binding with the claimed peptide and Rieu teaches away from a 15-mer by teaching a broad interactive region.

Applicants argue that the peptide of A7 does not have the claimed bioactivity and the specification teaches that unconjugated peptides inhibited cell adhesion poorly.

Applicants argue that the invention does not relate to sensor chips or to Plasmon resonance.

Applicants argue that there is no reason to combine the references.

Applicants argue that the prior art does not teach that the polymer inhibits the binding of leukocytes to ICAM-expressing cells.

Applicant's arguments filed 3/4/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 3-6) that the examiners assertion is no more than an invitation to try and there is no indication of which parameters were critical and there is no

direction as to which of many choices were likely to be successful, Rieu teach that the A-domain may be useful for treating hookworm infections and state that the A domain is a target for anti-inflammation therapeutics (page 2090). Importantly, Rieu teach that specific peptide fragments were assayed (figure 6). One of the peptides tested (A7 figure 6) corresponded to residues 232-245 and had the amino acid sequence NAFKILVVITDGEK. Rieu teach that the binding site comprised primarily peptide A7 (page 2089 first sentence of first complete paragraph, Figure 6). Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2nd column). Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK). Thus Rieu teach a specific peptide fragment from a specific protein. Therefore Rieu has identified a specific parameter (i.e. a specific peptide fragment from a specific protein) and furthermore has given an indication as to which parameter was likely to be successful - Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2nd column). Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK). Further, Figure 6b shows that A7 inhibits binding better than A1,A2,A3,A4,A5,A6,B2,A11,B5, and A12. Thus, the data and teachings point to the use of A7. Thus one would have a reasonable expectation of success based on the express suggestions of Rieu.

Although Applicants argue that there is no reasonable expectation of success regarding ICAM binding with the claimed peptide and Rieu teaches away from a 15-mer by teaching a broad interactive region, Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2nd column). Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK). Thus one would be motivated to couple such peptide via thiol

coupling to dextran as taught by Laplantine. In the instant case, the prior art expressly teach the hydrophilic polymer/polysaccharide as recited in claim 106. Thus there is a reasonable basis that the polysaccharide has the recited function. Further, the prior art suggest the peptide sequence as recited in claims 102,105. Thus there is a reasonable basis that the peptide has the recited function. It is noted that claim 106 expressly recites dextran and claim 105 recites a peptide sequence. If such components are not sufficient for the function it is unclear what would be required. In other words, it is contradictory to argue that the claims require A and B yet A and B do not have the recited function. With regard to the interactive region, Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2nd column). Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK). Section 2123 of the MPEP expressly states that alternative embodiments do not constitute a teaching away.

Although Applicants argue that the peptide of A7 does not have the claimed bioactivity and the specification teaches that unconjugated peptides inhibited cell adhesion poorly, it is first noted that the claims merely recite 'inhibits monocyte adhesion' and the claims do not recite any degree of inhibition. Applicants point to section 0138 which refers to 'poor' inhibition which suggests that there was in fact inhibition. Further, Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2nd column). Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK). Thus one would be motivated to couple such peptide via thiol coupling to dextran as taught by Laplantine. In the instant case, the prior art expressly teach the hydrophilic polymer/polysaccharide as recited in claim 106. Thus there is a reasonable basis that the polysaccharide has the recited function. Further, the prior art suggest the peptide sequence as recited in claims 102,105. Thus there is a reasonable basis that the peptide

has the recited function. It is noted that claim 106 expressly recites dextran and claim 105 recites a peptide sequence. If such components are not sufficient for the function it is unclear what would be required. In other words, it is contradictory to argue that the claims require A and B yet A and B do not have the recited function.

Although Applicants argue that the invention does not relate to sensor chips or to Plasmon resonance, the instant claims are drawn to a product. Whether or not the product is used in Plasmon resonance or any other application does not appear to be relevant. In other words, there is no basis to exclude certain prior art based on the application. As discussed in detail above the prior art suggest the claimed elements. Claim 102 and 105 recite hydrophilic polymer/polysaccharide. Claim 106 recites dextran. The prior art expressly teach dextran. Claim 106 recites that the polysaccharide is dextran but does not exclude any particular types or forms of dextran.

Although Applicants argue that there is no reason to combine the references, in the instant case, both Rieu and Laplantine are drawn to methods of identifying interacting regions between integrins and interaction partners. Rieu recognize a goal of mapping of the binding site (see page 2086 2nd column heading). Rieu teach a method in which peptides were adsorbed to plastic wells but notes that numerous peptides did not absorb adequately (page 2086 first paragraph). Laplantine teach a method in which selected peptides containing an additional N-terminal cysteine were immobilized on dextran through thiol coupling and used as part of a surface plasmon resonance analysis. Rieu teach that the A-domain may be useful for treating hookworm infections and state that the A domain is a target for anti-inflammation therapeutics (page 2090). Thus one would be motivated to identify the A-domain. Since the experiments of

Rieu were limited by the inability of certain peptides to bind one would be motivated to use other known methods to test direct binding. As discussed above, Laplantine teach such methods. One would have been motivated to combine the references to address the problem. Thus one would be motivated to address the problem set forth in Rieu. In fact, section 2143.01 of the MPEP states: "The court found motivation to combine the references to arrive at the claimed invention in the "nature of the problem to be solved" because each reference was directed "to precisely the same problem of underpinning slumping foundations." Id. at 1276, 69 USPQ2d at 1690. The court also rejected the notion that "an express written
motivation to combine must appear in prior art references...." Id. at 1276, 69 USPQ2d at 1690." Further, section 2143.03 of the MPEP states: "person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." Id. Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." Id. at ___, 82 USPQ2d at 1396."

Although Applicants argue that the prior art does not teach that the polymer inhibits the binding of leukocytes to ICAM-expressing cells, it is noted that the claims do not refer to leukocytes. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. Further, claim 106 expressly recites dextran which is taught by the prior art.

Related Prior Art

The prior art previously made of record (5/11/09) and not relied upon is considered pertinent to applicant's disclosure:

Arnaout WO 91/19511: Arnout teach SEQ ID NO:50 (comprises NAFKILVVITDGEK) (see claim 5 for example) and carriers for administering the peptides (claim 17).

Bocher et al (Journal of Immunological Methods 1997 v208 pages 191-202). Bocher teach the use of peptide-dextran conjugates compared to the use of peptide adsorbed onto immunoplates (abstract).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
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Examiner, Art Unit 1654